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The First Molecular Modelling and Graphics Society Electronic Conference

by

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Abstract

In this article we describe activities at the The First Molecular Modelling and Graphics Society Electronic Conference (MGMS EC-1) which was held on the Internet and World Wide Web in October 1996 [1]. MGMS EC-1 involved the presentation and discussion of scientific research results in a virtual conferencing environment which incorporated virtual replicas of many activities usually observed at a physical conference in addition to features unique to the electronic medium. Highlights of the scientific programme and technical developments in the design and use of these facilities are briefly described. A second electronic conference is planned for October 1997 [2].

Introduction

At the MGMS EC-1 event [1] presenters were able to display research results using a World Wide Web (WWW) presentation of text and graphics and could discuss the results within the context of an interactive software environment running on the Internet. Simply put a scientist was able to sit at their computer and view presentations and exchange comments with other scientists situated in their own offices or labs in other parts of the world. A variety of activities were possible including the ability to manipulate molecular structures, to submit and review resumes, to review exhibitor product descriptions and to carry out online searches of the proceedings.

MGMS EC-1 was held on the Internet from Oct 7-18, 1996 [1] with entry to the site via an extensive set of WWW pages accessible from the front of the WWW site shown in Figure 1. The conference was sponsored by Elsevier, the Molecular Graphics and Modelling Society (MGMS), Oxford Molecular, MSI, Springer-Verlag, Wyeth-Ayerst, NASA-Ames and GlaxoWellcome. The event attracted close to a hundred presentations and over two hundred participants. The conference was served both from a UK location (The University of Oxford) and the US (S.U.N.Y. and Wesleyan University) with continuous real-time mirroring of the interactive environment. A similar event is planned for for October 1997 [2]. In this article we give an overview of the feautures, events and news of the first conference whereas a more detailed analysis of the software environment and its use is given elsewhere [3].

Overview

MGMS EC-1 was a fully international event open to all members of the scientific community and covered a broad range of disciplines related to molecular modelling, graphics and simulation methods and applications including section areas and conveners in the following topics: Protein Structure (Rod Hubbard, University of York, UK); Membranes and Membrane Proteins (Alan Robinson, University of Oxford, UK); Computational Nanotechnology (Al Globus, NASA-Ames, USA); Protein Folding (Jeffrey Skolnick, Scripps Institute, USA); Modelling of In Vivo Activity (Edward Hodgkin, Wyeth-Ayerst Research, USA); Knowledge-based Library Design (Mike Hann, GlaxoWellcome, UK); Surface Science (Donald Brenner, North Carolina State, USA); Host-guest interactions (Jon Essex, Southampton University, UK); Carbohydrates and Protein-Carbohydrate Interactions (Anne Imberty, CNRS, France); Enzyme Mechanisms (Guy Grant, University College Dublin, Ireland); Stochastic Methods for Conformational Sampling (Robert Topper, The Cooper Union, USA); Nucleic Acids (David Beveridge, Wesleyan University, USA); Quantum Chemistry (Tim Clark, University of

(David Beveridge, Wesleyan University, USA); Quantum Chemistry (Tim Clark, University of Erlangen, Germany); Structure-based Design (David Winkler,CSIRO, Australia); Visualization (Art Olson,Scripps Institute, USA); Perspectives (Graham Richards, University of Oxford, UK).

Presenters in each section were able to opt to submit a non-permanent presentation like a normal conference poster or could submit a presentation paper which was refereed and considered for publication in the Journal of Molecular Graphics using the Internet itself for post-conference refereeing.

Presentations were prepared in Hypertext Markup Language (HTML), graphics (GIF,JPEG) and other web-compatible formats (VRML,Java,PDF) so that participants could view the papers via the World Wide Web. Aid and consultation was provided via an electronic hot-line to participants in the weeks prior to the event to help them with any difficulties involved in their preparations. Materials were deposited via ftp to the conference site after which they were entered and indexed in the conference library shown in Figure 2 and mirrored.

Prior to the conference electronic registration was achieved via WWW-based forms. The registration process was used to construct a registrant database for the conference which generated the conference mailing list and handled assignment of registration characters, userids, passwords.

During the conference discussions took place via the Internet in real-time using a virtual conference centre based on a MOO (multi-user domain, object-oriented) and via Internet-accessible electronic mailing lists. Trial sessions for those not familiar with MOOs were held at the start of the conference. Before the conference, a timetable for MOO discussion sessions of each section was posted and these real-time discussions formed an integral part of the conference. The MOO could be navigated around by buttons located in the top frame bar shown in Figure 3 allowing viewing of objects in HTML and conversation via the facilities illustrated in the Figure which is based on an example tutorial page.

The Conference also featured a Virtual Trade Center (Figure 4) where commercial vendors and sponsors were able to display their goods and services and provide software demonstrations and an Employment Centre where resumes could be both posted and reviewed and interviews scheduled. A molecular gallery sponsored by MSI was created to automatically accept entries created by participants with Web Lab Viewer with the entry shown in Figure 5 being the competition winner of Ana Poveda of the University of Madrid.

Technology

For MGMS EC-1 we established a WWW forms-based registration facility that automated the receipt of user information, the addition of the user to the mailing list or interactive environment and the notification of the password and userid to the user. The front pages of the site (see Fig. 1) were open in the months prior to the conference to process the registrations and to provide user help and information via the WWW pages and a mailing-list based "hot-line" for user support. These modifications significantly aided the smoothness of conference preparations and commencement.

The conference WWW site was reproduced in "light" and "heavy" modes in addition to a "standard" non-frames version. The "light" version was text-oriented and designed for faster access over a slower dialup line whereas the "heavy" version contained pages with frames, maps and graphical icons. Maps based on the metaphor of the arrangement of spaces in a physical conference centre were provided to different areas of the site that could be visited to engage in varied activities from lectures to job queries to the reading of discussion transcripts in the archive library.

To aid the reduction of connection problems and transatlantic lag, a full mirroring operation was performed in which a complete copy of the WWW site and the associated interactive environment at the European site at Oxford was replicated and regularly updated at the US sites at S.U.N.Y., New York and Wesleyan University in Connecticut. The interactive environments running in the UK and US were tied together so that users logged into the sites on different sides of the Atlantic could follow the activities of all users based on information communicated between the servers on incremental interactive changes to the environments. Server response was nevertheless slow at times and often due to network delays on the Internet. Enhancing access speed is an important priority area needing further improvement for future events.

future events.

During MGMS EC-1 we emphasized realtime discussion sessions as part of a scheduled programme and initiated an effort to make increased use of the WWW as an interface into the interactive environment and to increase the integration of the WWW and the MOO. Auditoria were set up which were accessible from a WWW page showing the current transcript of conversation in the room since the start of the current session. Questions could be entered by users into a box on the WWW page and subsequently queued for submission to the current speaker. A "Listen & Talk" button provided an active connection where users could discuss in realtime chat mode via a scrolling WWW page. An attendee could also use other buttons to obtain listings of currently logged-in users, to contact them directly, to observe their descriptions or photo (as illustrated in Figure 6) or to compose a mail message, all via WWW pages. Upon completion of a session a saved transcript was automatically transferred to a WWW archival library page where it could continue to be viewed and could be annotated by any subsequent reader. In addition to formal sessions casual areas such a Virtual Bar (Figure 7) were provided for informal social interaction. Users could create their own customised "hotel" rooms which they could use for smaller meetings or chat. Real coffee was provided courtesy of Oxford Molecular in the virtual coffee shop although since the coffee had to be delivered by regular mail users had to rely on local supplies to wake up for their morning sessions! However, if they needed some diversion before joining a session, an applet-based game of Othello or Asteroids was available at the shop.

Scientific Program

The scientific program consisted of sixteen sections covering a wide range of topics in molecular modelling and graphics. There were around one-hundred presentations of which approximately 30 were considered as papers for the Journal of Molecular Modelling and Graphics whereas the remainder of the presentations were served as electronic posters. Only a brief overview of the flavour of the presentations will be presented here.

Graham Richards presented a perspective of his group's work at Oxford including the prediction of protein structure; the design of enzyme inhibitors; the design of molecules showing selective binding to DNA and the development of methods to assist medicinal chemists in drug design. A question and answer session was held in which participants were able to field questions to Professor Richards via a queueing mechanism which were forwarded in turn via the session moderator. A similar session was also held with the group of Harel Weinstein on their perspectives in molecular recognition and signal transduction except in this case several of the Weinstein group members were present simultaneously to field questions from the audience.

Al Globus hosted a session on nanotechnology and along with his coworkers at NASA-Ames presented an extensive description of their ambitious computational nanotechnology program. Both the work at NASA on the design of nanotube gears and that of Brenner on fullerene-based gears stimulated a discussion on the weakness of competing designs and the challenges and insights obtained from simulation on the gear design process. Figure 8 shows a sample snapshot from a simulation on Carbon Nanotube-Based Gears by Globus and coworkers at NASA. In the section on surface science MD simulations of liquid crystal molecules on polyimide monolayers were presented by Yoneya of Hitachi, Japan.

The conformational sampling papers of the section of Robert Topper focused on stochastic methods including kinetic Monte Carlo applied to zeolites (Auerbach), Langevin Dynamics simulations of protein folding (Paterlini,Troyer, Cohen and Ferguson), the application of information theory to the J-walking method (Doll and Freeman) and the introduction of a 4D->3D step and an MD step into DGEOM distance geometry methods (Spellmeyer, Wong, Bower and Blaney).

Keasar, Elber and Skolnick proposed a combination of the two approaches of homology modeling and global energy optimization for protein structure prediction asserting their coupling improves the sampling of native-like conformations. Zheng, Cho, Vaisman and Tropsha proposed new algorithms for sequence-structure compatibility (fold recognition) searches in multi-dimensional sequence-structure space. The algorithm incorporated tessellation of a protein to generate an aggregate of space-filling, irregular tetrahedra, or Delaunay simplices followed by statistical analysis of their quadruplet residue

irregular tetrahedra, or Delaunay simplices followed by statistical analysis of their quadruplet residue compositions. Erman, Bahar and Jernigan described the development of coarse-grained folding potentials which included both long and short range interactions.

In the host-guest section of Jon Essex Guilleux, Joffre, Babiau, Schmit, Pautrat and Lerner described modelling of the stability of beta-cyclodextrin and diphenylhexatriene molecular nanotubes. For the enzyme mechanism section Zuegg, Purisima and Cygler analysed the conformations of triglyceride in the binding site of Candida rugosa Lipase.

Tim Clark presided over the quantum chemistry section. With his coauthors Gedeck, Herz and Lanig he discussed the use of harmonically-constrained atoms to enzyme active site models and obtained good geometric results upon applying the technique to a series of carboxypeptidase A - inhibitor complexes. Griffith, Yates, Bremmer and Titmuss described a quantitative investigation of the transannular amine-ketone interaction in medium-sized heterocycles. Patrick O' Malley calculated the 1H, 13C and 17O hyperfine coupling tensors for the p-benzosemiquinone anion radical directly using hybrid density functional methods. Excellent agreement between experimentally determined tensor values and theoretically calculated ones were reported. Proton tensors for solvent hydrogen bonding interactions with an alcohol solvent were also well reproduced.

The WWW is particularly suited to the visualization of structural information and the section on this topic included the description of image libraries of biological molecules and the use of Virtual Reality Markup Language by Juergen Suehnel whereas William Carson used extensive use of VRML and audio files in his imaginative presentation on the sound of protein sequences and his search for their harmonious sonification. A more familiar topic of hydration visualisation was treated by Pitera and Kollman who have developed insightful methods of water shell analysis such as the depiction of mean dipolar vectors of water around N-methyl acetamide shown in Figure 9.

Mike Hann of Glaxo presided over discussions on knowledge-based library design reflecting the growth in importance of the use of combinatorial chemistry in the generation of new lead compounds in the pharmaceutical industry. Lewell and Smith showed that building central databases of common monomers with pre-defined clusters and chemical descriptors for similarity/diversity searching and pre-screening were extremely valuable in generating ideas and cuting down pre-processing time. Good, Pickett and Lewis described a host of enhancements to the product-based methods for determining molecular diversity applied by the Chem-Diverse software. These included direct reagent selection from product diversity, the application of more advanced diversity measurement functions incorporating both shape and pharmacophore key information, and full pharmacophore profiling of entire molecular databases. Other papers covered the use of conformational focussing, topological indices and simulated annealing in the design of targeted libraries. The modeling of in vivo activity section of Edward Hodgkin covered the Estimation of Caco-2 Cell Permeability Using Calculated Molecular Properties (Camenisch, van de Waterbeemd and Folkers)) and the Transport of Novel CNS Compounds Across The Blood-Brain-Barrier, an In-vitro, In-vivo Correlation (Ribadeneira, Eyermann, Chi, Shen and Huang.)

Anne Imberty hosted the section on carbohydrates which included a detailed review of protein-carbyohdrate interactions as studied by NMR and molecular modelling, an analysis of the internal motions and hydration of sucrose in diluted water solution by Engelsen and Perez and MD simulations of the inclusion of mono- and disubstituted benzenes in beta-cyclodextrin by Manunza, Deiana, Pintore and Gessa. In the nucleic acids section Slickers and Suehnel presented MD simulations of an antibiotic (SN6999) in the minor groove of DNA that indicated that a sliding of the ligand in the minor grove was possible.

The Protein structure session saw presentations on the Homology Modelling of The Human Interlukin-7 Receptor Complex (Kroemer & Richards), Modelling of the Shock Protein-Binding Molecule 15-Deoxyspergualin, (Hazar, Yuriev, Bigger & Orbell), Molecular Dynamics Simulation of a Protein Crystal under Rotational Symmetry Boundary Conditions (Yoneda) and The Random Coil State of Proteins (O'Connell, Wang, Hermans and Tropsha). The membrane section also had a protein emphasis with several papers presented on ion channel modelling including the Simulation of Hairpin-bilayer Interactions in the Presence of a Transmembrane Potential (Biggins & Sansom) and a Molecular Dynamics study of water and sodium ions in models of the pore region of the Nicotinic Acetylcholine

Dynamics study of water and sodium ions in models of the pore region of the Nicotinic Acetylcholine Receptor (Smith & Sansom). The model of the pore of the Nicotinic Acetylcholine Receptor in its open state presented in the Smith & Sansom paper is shown in Figure 10. The paper of Smart on the Analysis of Pore Dimensions in Ion Channels provoked a long and spirited discussion of the correct electrostatic treatment of channel conductance properties.

Discussion - New Activities

As MGMS EC-1 lasted for only two weeks the question was naturally raised on whether a more continuous set of activities would be useful. Efforts are currently getting under way to supply a Molecular Modelling & Graphics Network Live! service [4] consisting of a WWW-based scientific resource in which members may access an interactive environment on a continuous basis to participate in online scientific events including lectures, discussions, poster sessions, journal clubs, collaborative scientific projects, structural and informatic resources, other scientific projects, and a Job and Trade Centre. These activities will be available on a year-round basis to subscribed members and it remains to be seen what the response and demand to such a service will be and how it should be refined.

A second conference in molecular modelling & graphics [2] will be held from Oct 6 - Oct 17 1997 and will feature many of the activities mentioned in this article. We also anticipate new developments including use of the Java programming language to provide more sophisticated user interfaces and the offering of audio-based options for presentations. The interested reader is urged to check the WWW site frequently to keep up on developments and news.

References

1. The First Molecular Graphics and Modelling Society Electronic Conference (MGMS EC-1), Oct 7 -18, 1996, http://bellatrix.pcl.ox.ac.uk/mgms/.

2. The Second Molecular Graphics and Modelling Society Electronic Conference (MGMS EC-2), Oct 6 -17, 1997, http://www.vei.co.uk/mgms97/. 3. Tennison, J., Doughty, S.W., Parretti, M.F. & Hardy, B. (in preparation) Integrating Text-Based Virtual Environments with the World-Wide Web: Experiences with Electronic Conferences. In C.P. Hand (ed.) Objects, Hypermedia and Virtual Environments. 4. The Molecular Graphics and Modelling Network Live! Service, http://www.vei.co.uk/mgmn/.

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Figure 9. Visualization of Mean dipolar vectors of Water around N-methyl acetamide; Jed Pitera and Peter Kollman, University of California San Francisco.

Figure 10. Model of the pore of the Nicotinic Acetylcholine Receptor in its open state; Graham R. Smith & Mark S. P. Sansom, University of Oxford.

MGMS EC 1

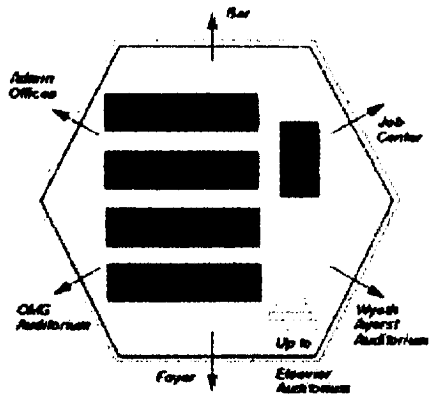
WebLab Information Available

Click to register, or Click the image to enter ...

Click here for Conference Interactivity

To exit frames at any point click

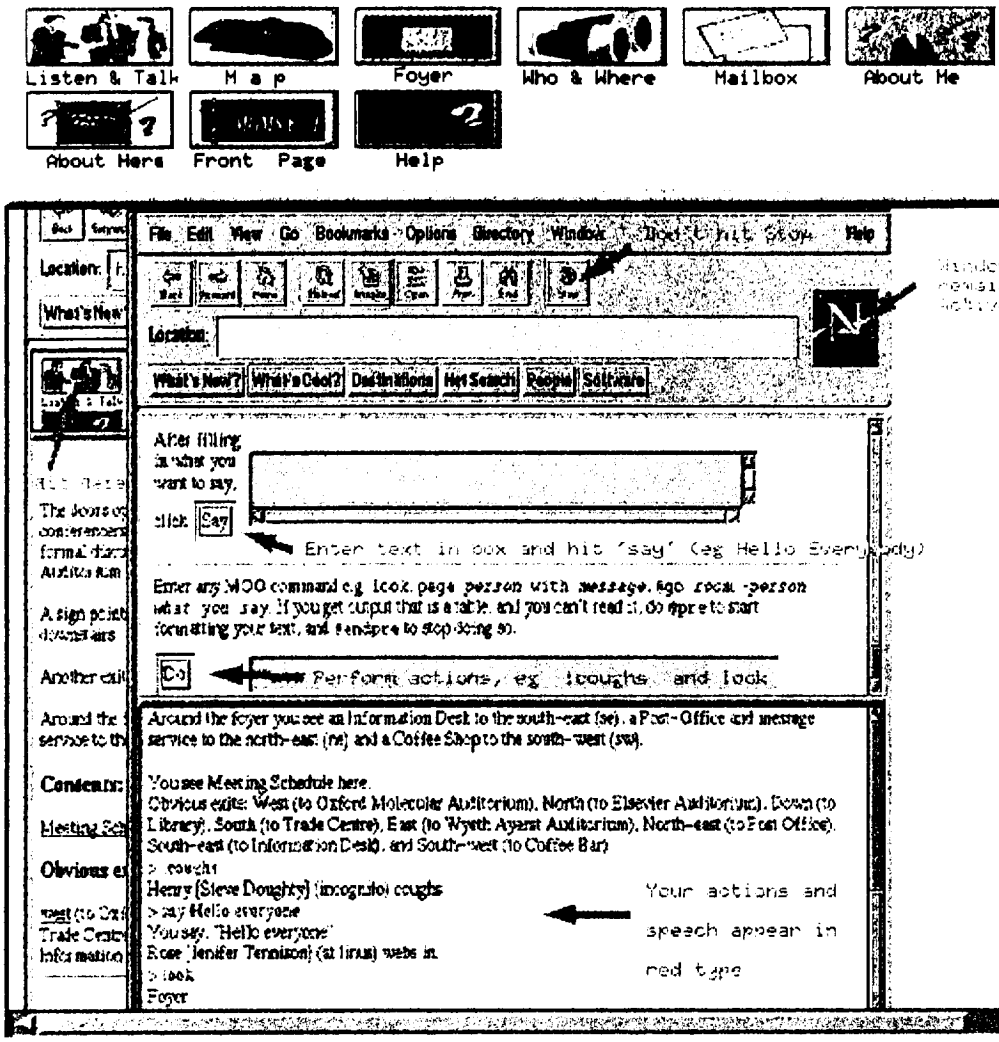
Search Info Help Software WESLEYAN

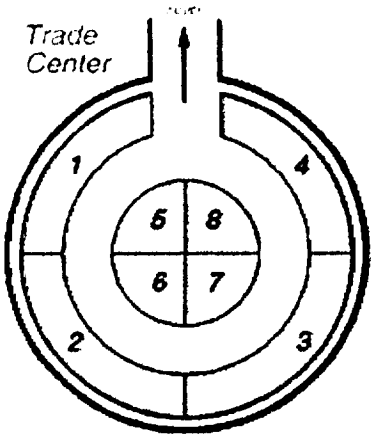


By Authors

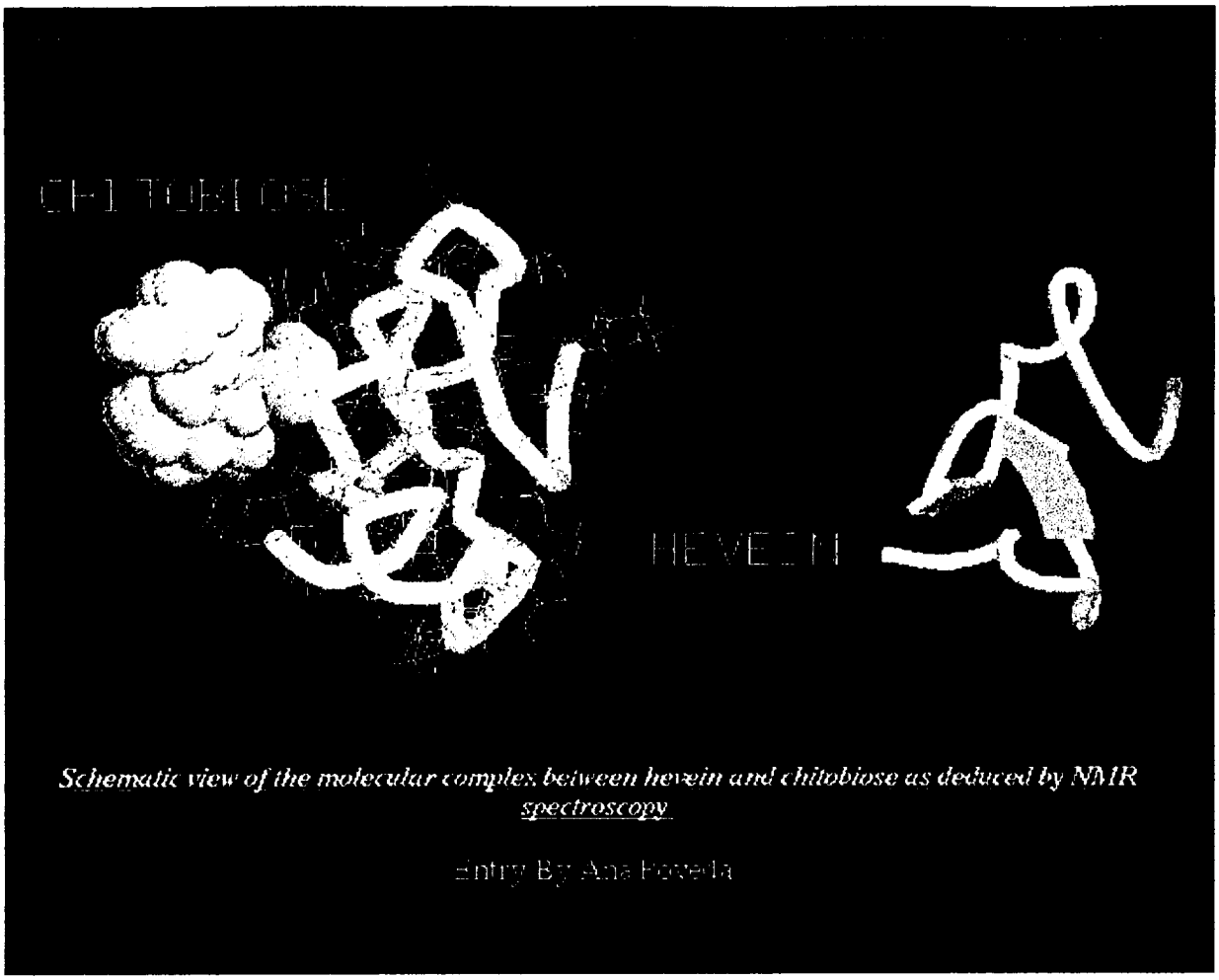
Library Interactive (MOO)

1. Protein Structure
2. Nucleic Acids
3. Membranes and Membrane Proteins
4. Cancelled
5. Computational Nanotechnology
6. Protein Folding
7. Modelling of In Vivo Activity
8. Knowledge- based Library Design
9. Surface Science
10. Host-Guest Interactions
11. Carbohydrates and Protein-Carbohydrate Interactions
12. Enzyme Mechanisms
13. Stochastic Methods for Conformational Sampling
14. Quantum Chemistry
15. Structure-based Design
16. Cancelled
17. Visualization
18. Perspectives in Molecular Modelling


Listen & Talk
Map
Foyer
Who & Where
Mailbox
About Me
About Here
Front Page
Help
File Edit View Go Bookmarks Options Directory Window Don't hit Stop Help
Location:
What's New? What's Cool? Destinations Net Search People Software
After filling in what you want to say, click Say
Enter text in box and hit 'say' (eg Hello Everybody)
Enter any MOO command e.g. look page person with message. goto room -person what you say. If you get output that is a table, and you can't read it, do ;pre to start formatting your text, and ;endpre to stop doing so.
Go
Perform actions, eg coughs and look
Around the foyer you see an Information Desk to the south-east (se), a Post-Office and message service to the north-east (ne) and a Coffee Shop to the south-west (sw).
You see Meeting Schedule here.
Obvious exits: West (to Oxford Molecular Auditorium), North (to Elsevier Auditorium), Down (to Library), South (to Trade Centre), East (to Wyeth Ayerst Auditorium), North-east (to Post Office), South-east (to Information Desk), and South-west (to Coffee Bar)
> coughs
Henry (Steve Doughty) (incognito) coughs
> say Hello everyone
You say, "Hello everyone"
Rose (Jenifer Tennison) (at linux) webs in.
> look
Foyer
Your actions and speech appear in red type



1. Oxford Molecular Group
2. Molecular Simulations Inc.
3. Wyeth-Ayerst Research
4. Springer
5. GlaxoWellcome plc.
6. NASA
7. Greenlea Communications Ltd.
8.



Schematic view of the molecular complex between hevein and chitobiose as deduced by NMR spectroscopy

Entry By Ana Poveda

barry [Dr Barry Hardy] (webbed)

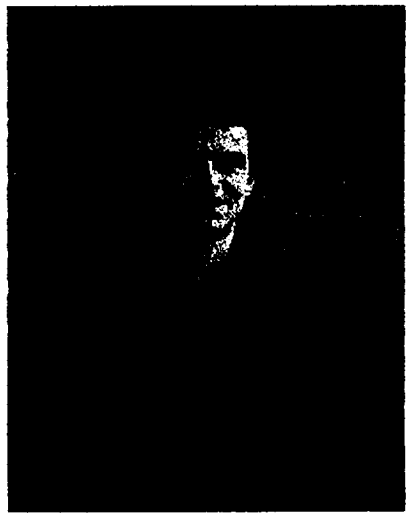
5ft 10. Dark Hair. Brown Eyes. Say hello – he can be friendly :)

Location:

Bar

Contents:

Schedule of meetings and Schedule of meetings



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